





Corneal Crosslinking Without Epithelial Removal

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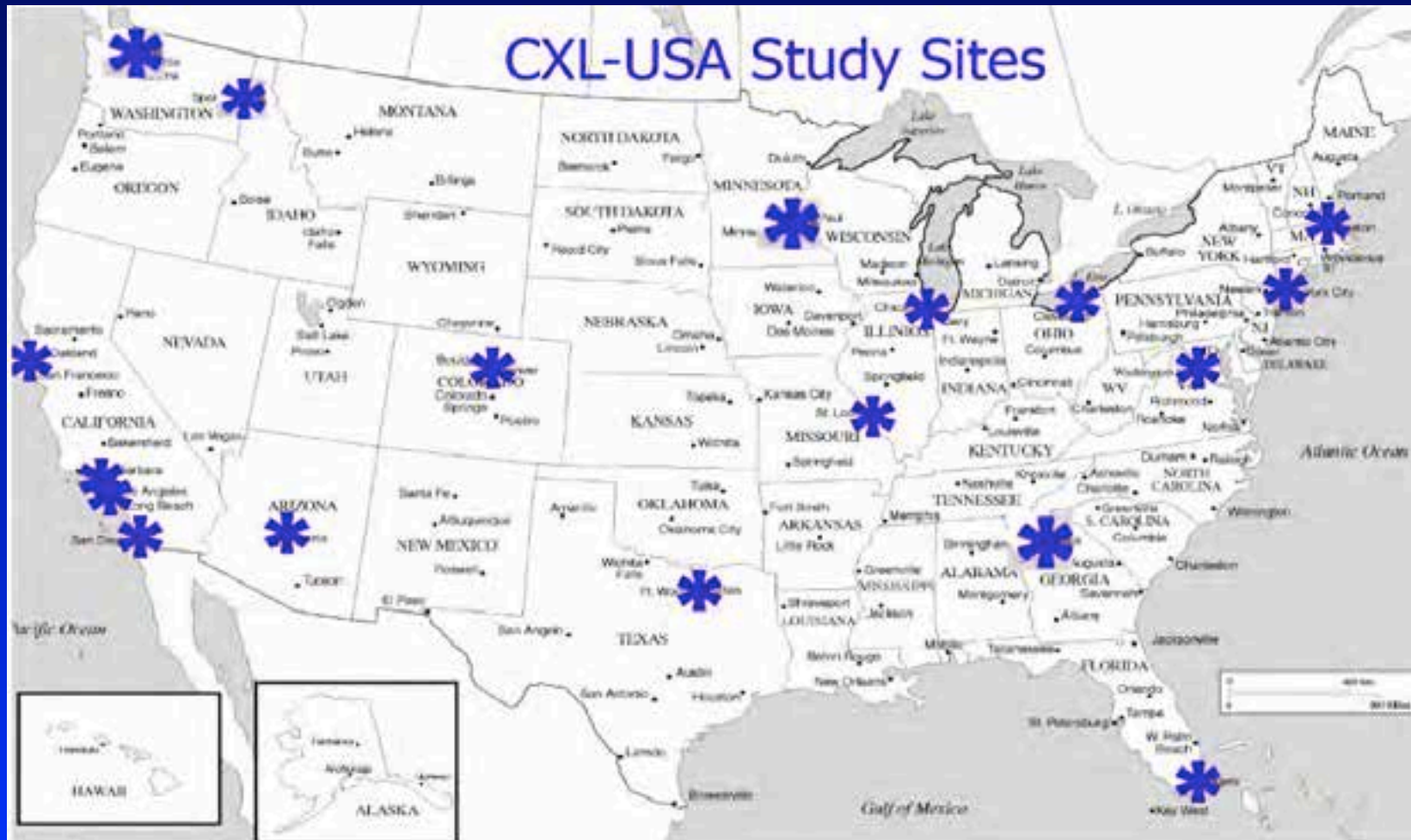
Financial Disclosures

- Abbott Medical Optics
- Alcon Laboratories
- Avedro
- Calhoun Vision
- Cambium Medical Technologies
- CXL Ophthalmics
- EyeYon
- Hydrolenz
- Intelon
- Ocumetrics
- Ophtec
- Primisight
- TearLab

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Methods



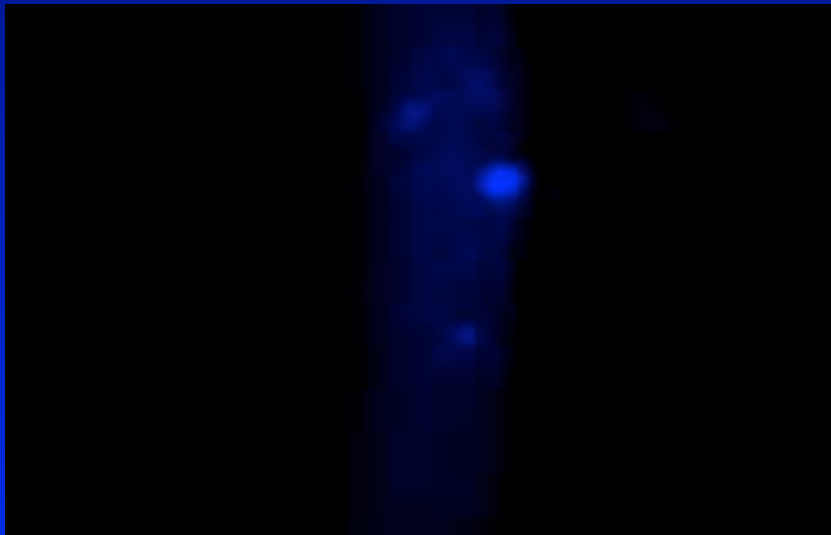
Methods

- Prospective, observational study
- Novel riboflavin formulation and loading technique¹
- Physician verification of riboflavin concentration, location, and homogeneity at 20 min. with additional loading as needed (5-10 min)
- 12mm diameter light
- No riboflavin during UVA exposure
- Pulsed UVA
- 4 mW/cm²

¹Patented riboflavin solution with optimized osmolarity, pH, concentration, nontoxic additive and delivery system developed by CXL Ophthalmics

Ex Vivo Rabbit Corneas

Commercially Available
Formulation



ParaCel 4 min. and VibeX 6 min. per label

CXLUSA Formulation



CXLUSA formulation and loading sponges 10 min.

Independent study performed by Absorption Systems, Inc., San Diego, CA, reported October 13, 2015

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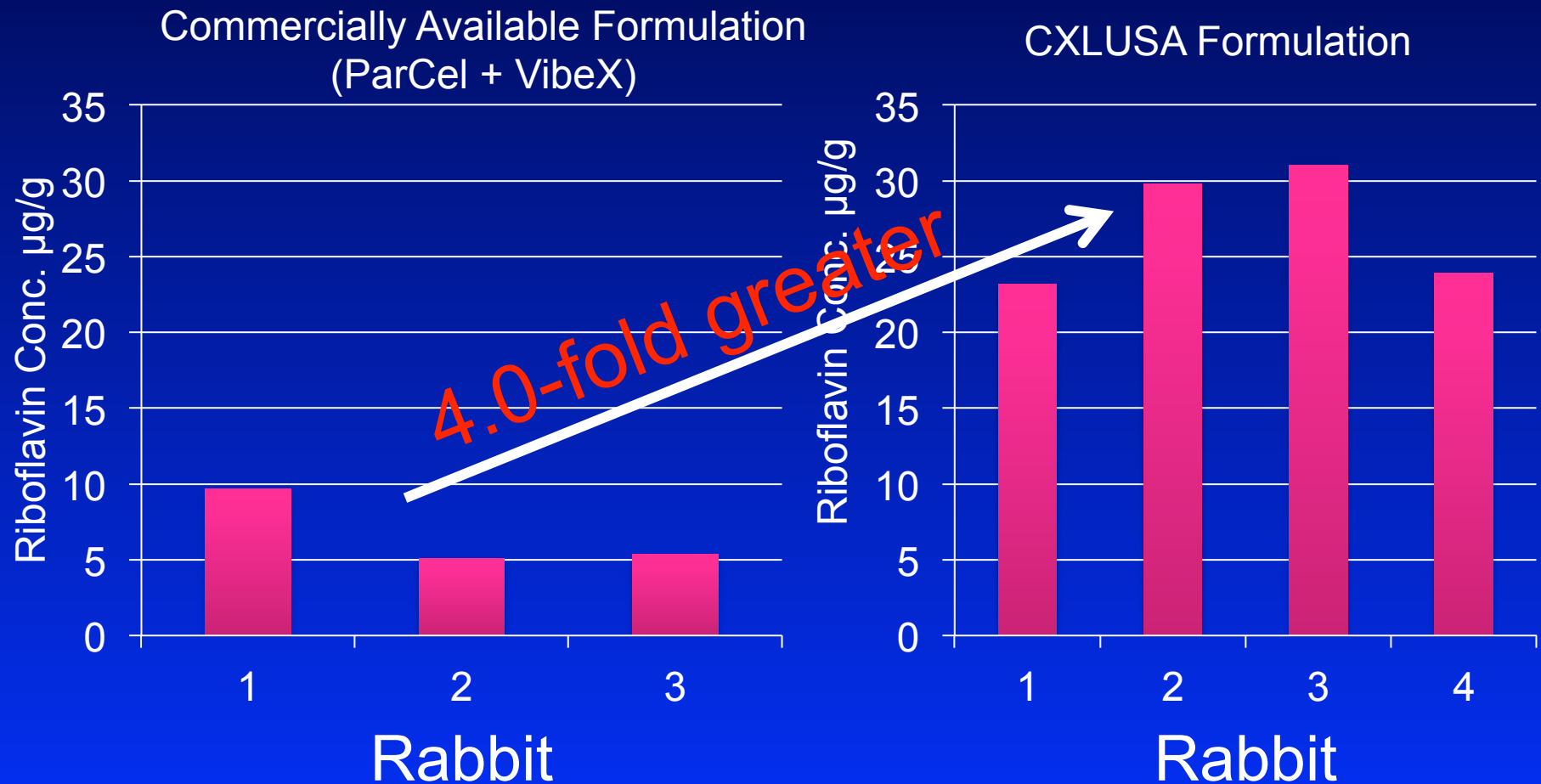


CXLUSA formulation and loading sponges 10 min.

Independent study performed by Absorption Systems, Inc., San Diego, CA, reported October 13, 2015

Corneal Riboflavin Concentration

($\mu\text{g/g}$ at 20-25 min.)



Liquid chromatography/tandem mass spectrometry

Independent study performed by Absorption Systems, Inc., San Diego, CA, reported October 13, 2015

Inclusion Criteria

- Keratoconus, PMD, ectasia, FFKC
- 8-yo min.
- CT_{\min} : 300μ

Enrollment

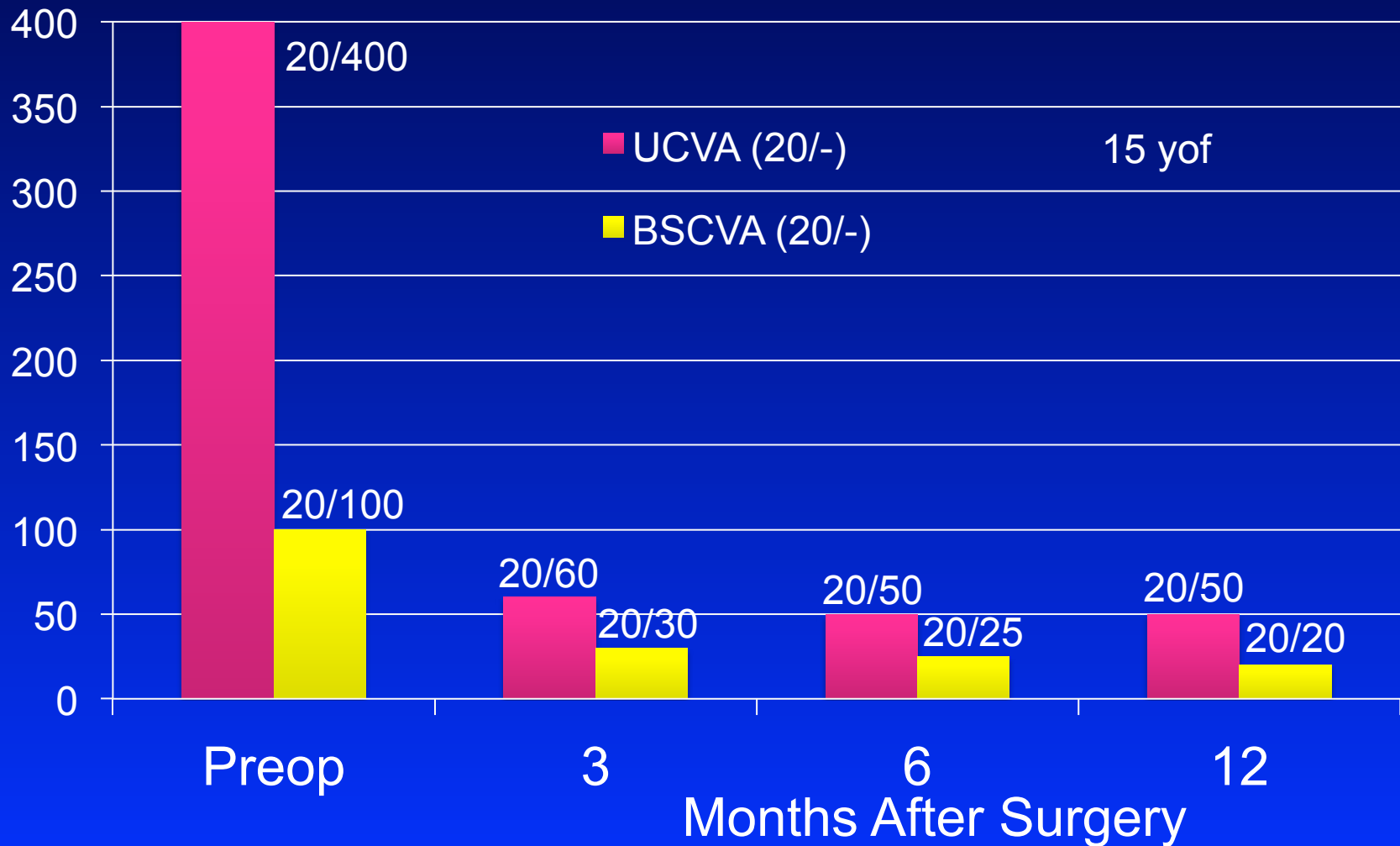
- October 17, 2013-April 26, 2016
- 608 eyes with ectatic disease (10-65 yo)
 - » Keratoconus: 512
 - » Ectasia: 80
 - » PMD: 16
- CTmin: 302 μ
- Database freeze 11/17/16

Interim Analysis

- Keratoconus or ectasia (excluding PMD)
 - » 592 eyes total
 - » 295 eyes with 12-month exams
 - » 97 eyes with 24-month exams
 - » 79 eyes (consistent cohort) with
 - 3, 6, 12, and 24-month exams
 - UCVA, MR, BSCVA, and Pentacam

Subject ATL-003

Keratoconus

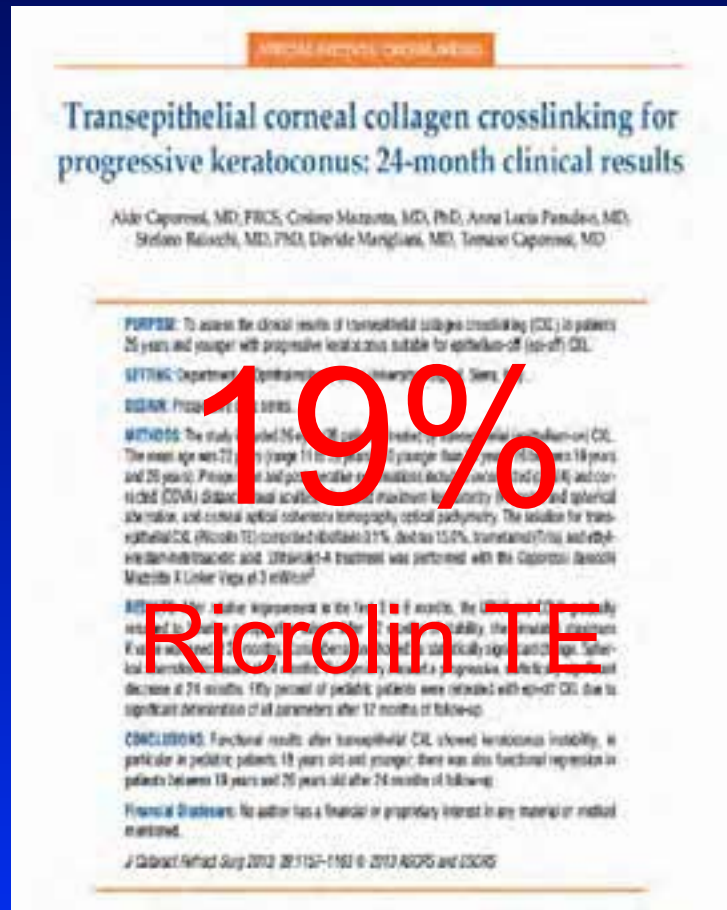


12-Month Followup

n=295

Parameter	Preop	12 mos	Change	%
UCVA (20/-)	148.3	110.5	~1line	
CDVA (20/-)	34.8	28.3	~1 line	
Kmax	56.14	55.71	-0.44	
Total HOA	1.262	0.886	-0.408	-29.8
Total Coma	1.041	0.718	-0.342	-31.1

Will We See Progression After One Year?



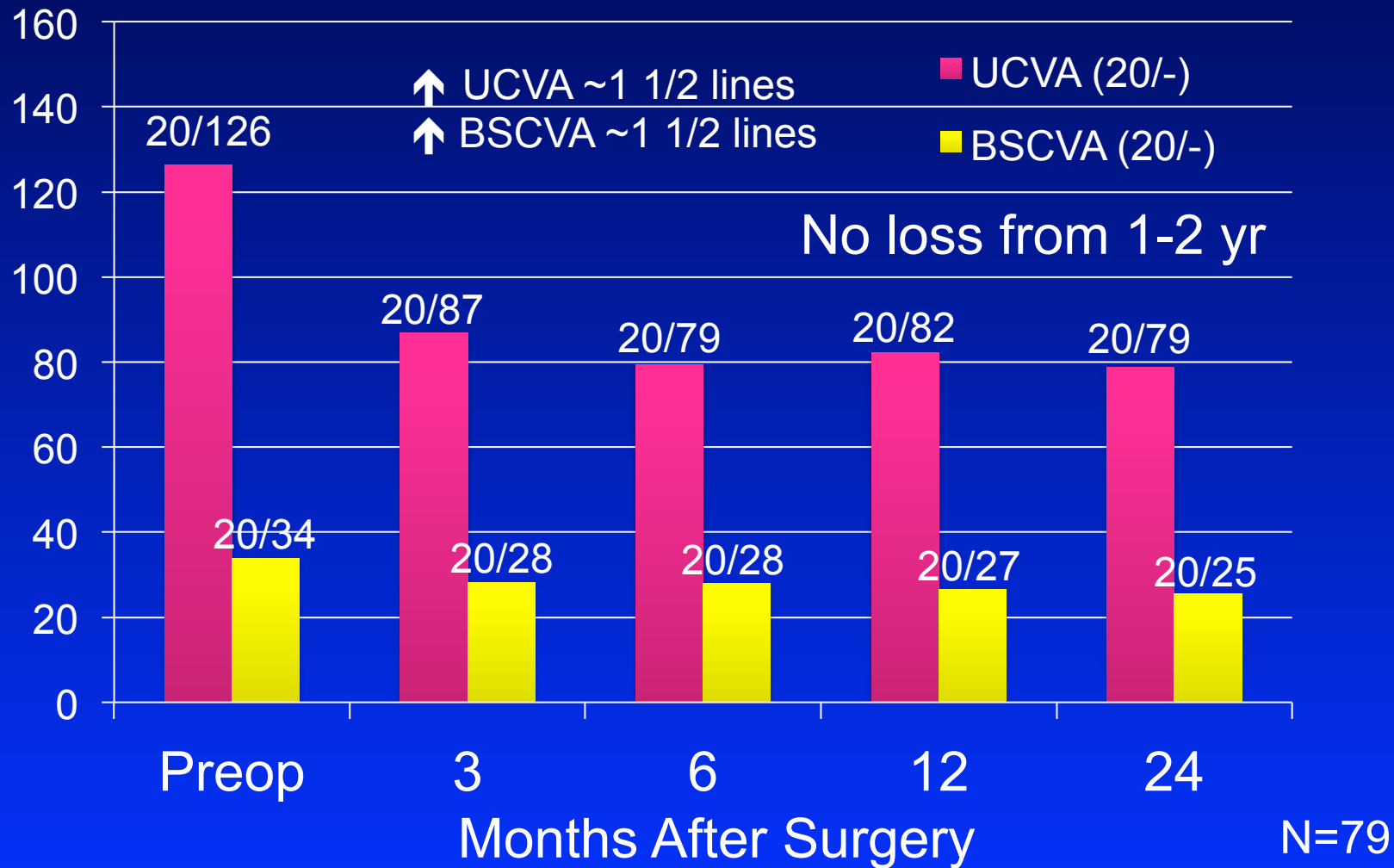
Caporosi et al. JCRS 2013;391:1157



Soeters et al., AJO 2015;159:821

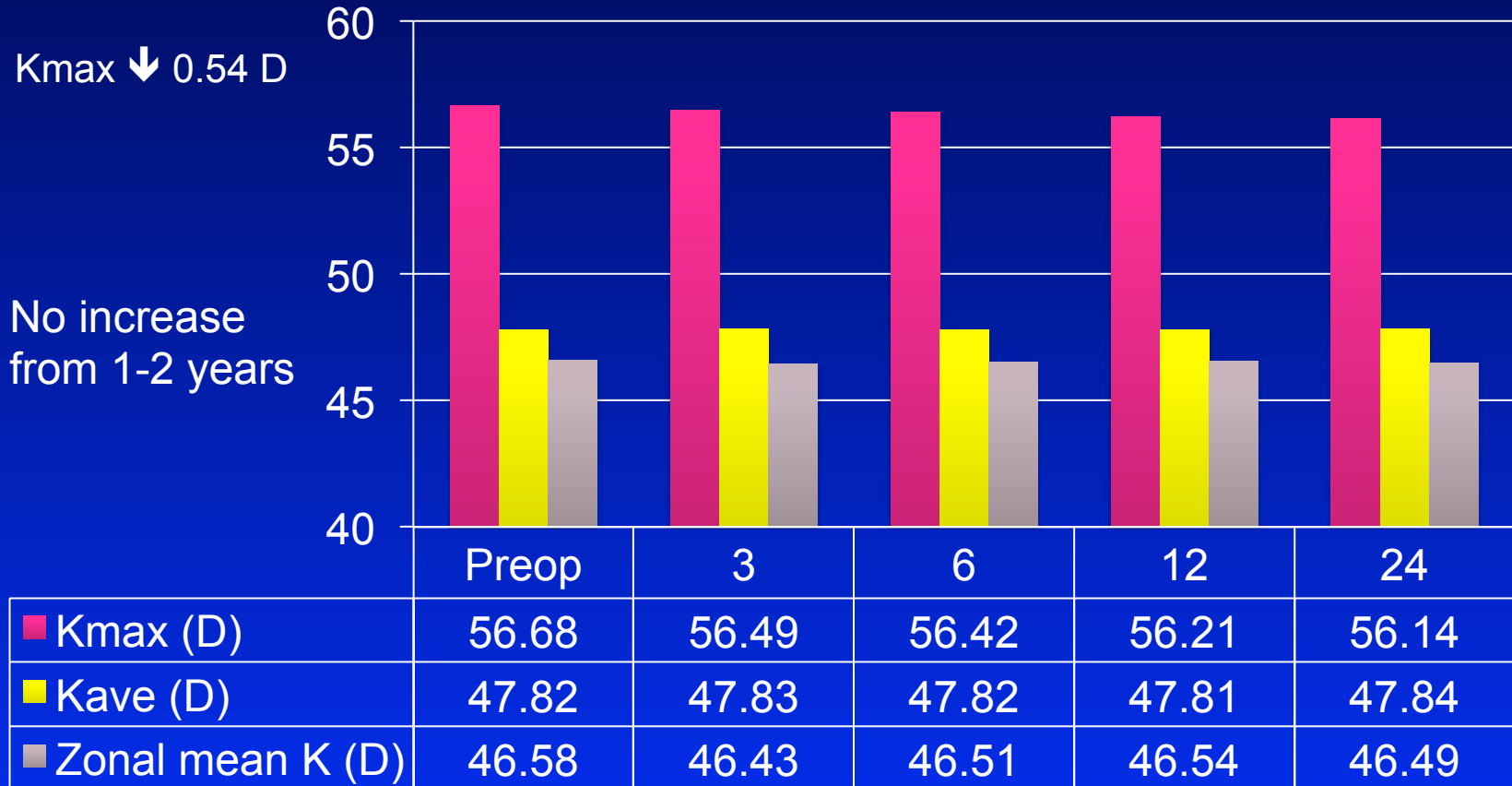
Visual Acuities

Consistent Cohort at 24 Months



Topography

Consistent Cohort at 24 Months

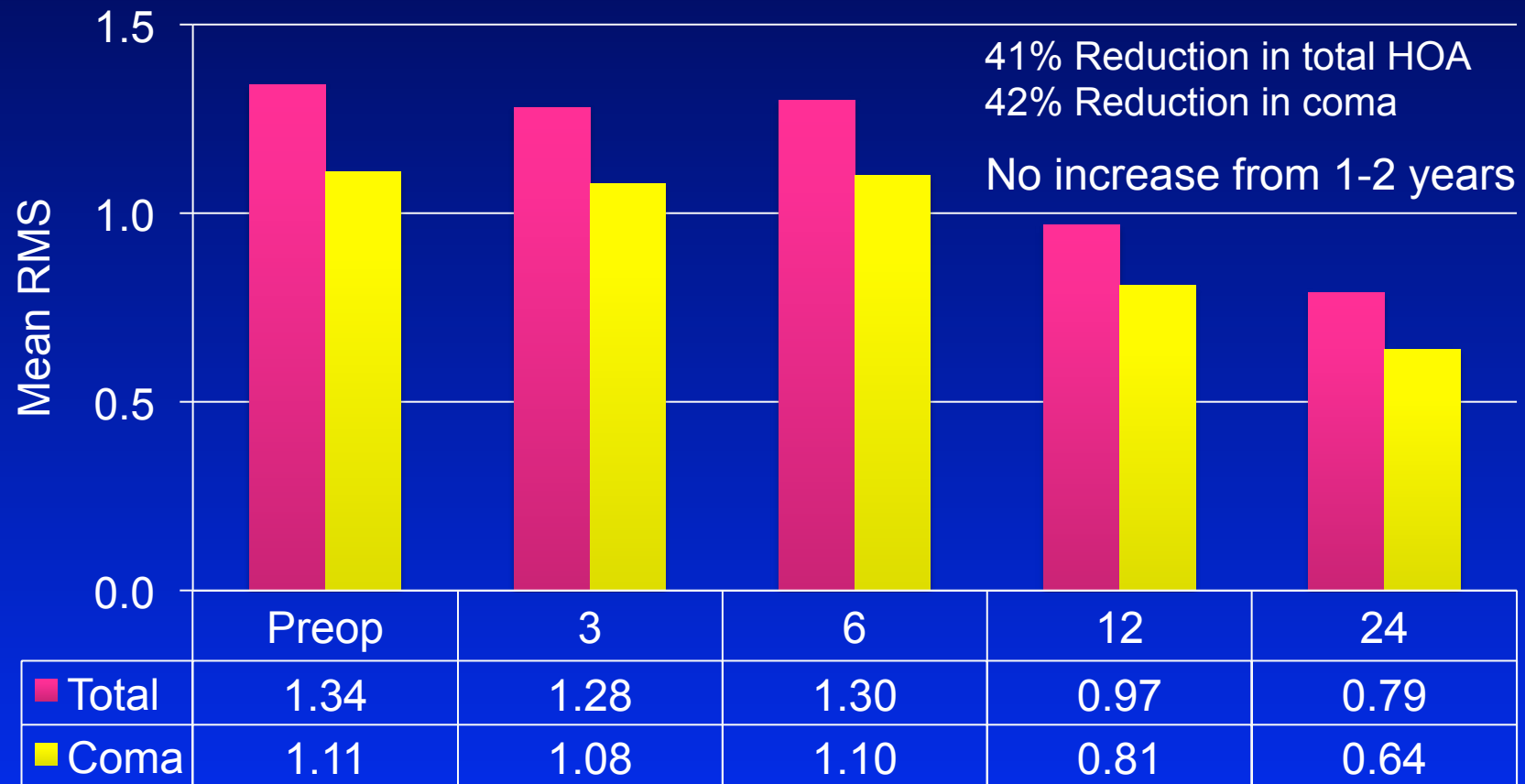


Months After Surgery

N=79

High-Order Aberrations

Consistent Cohort at 24 Months

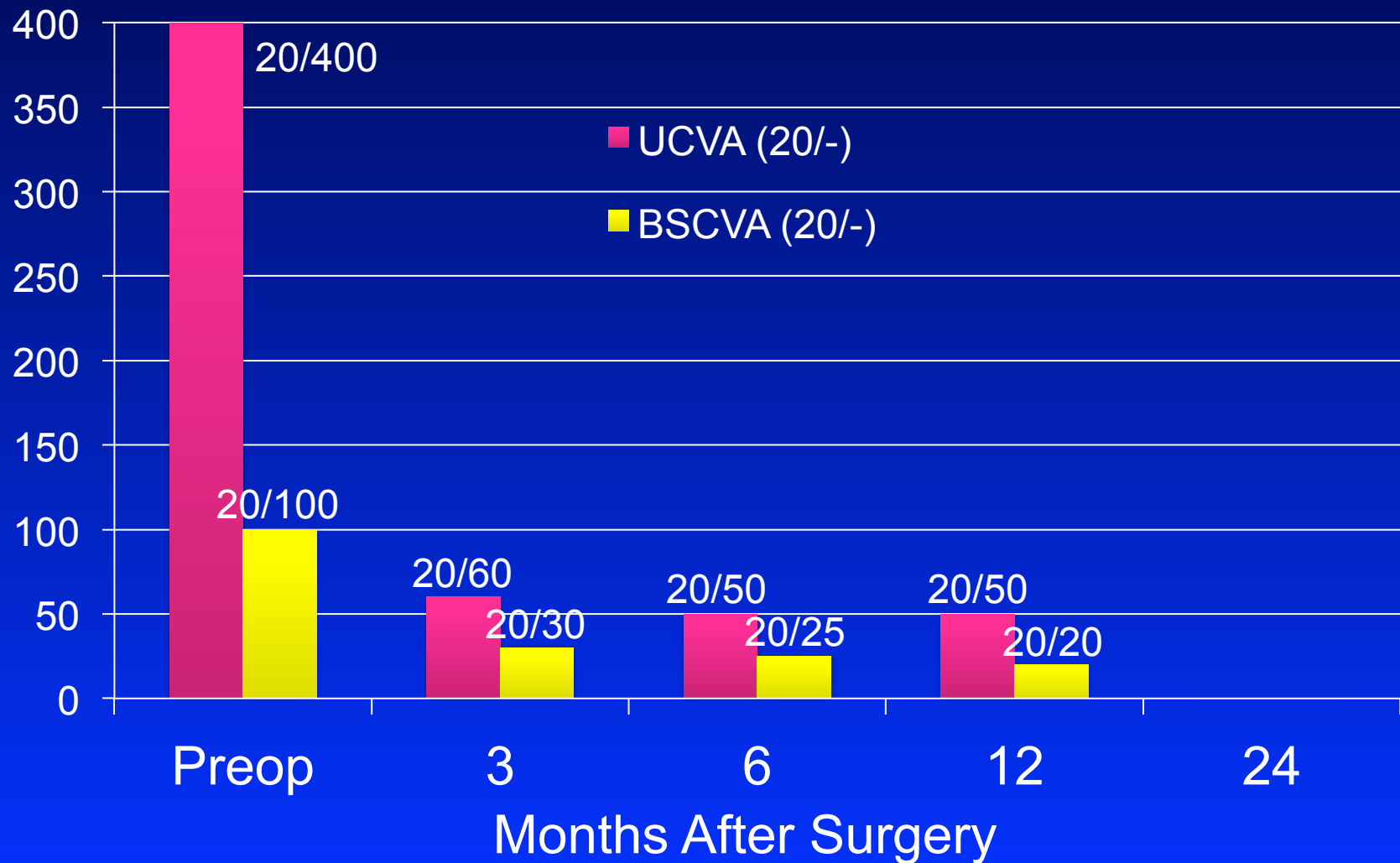


Months After Surgery

N=79

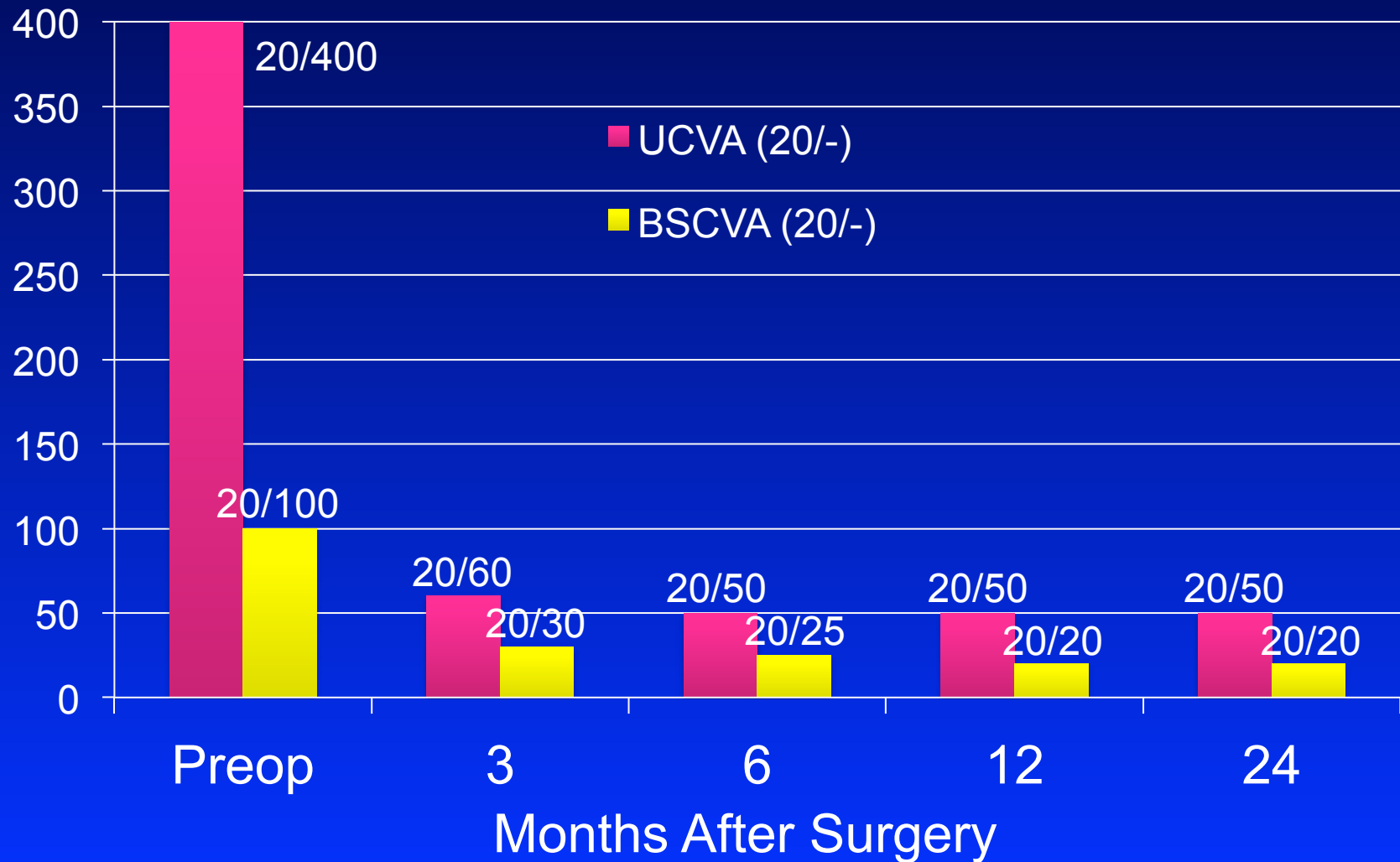
Subject ATL-003 OD

14 yof with Keratoconus



Subject ATL-003 OD

14 yof with Keratoconus

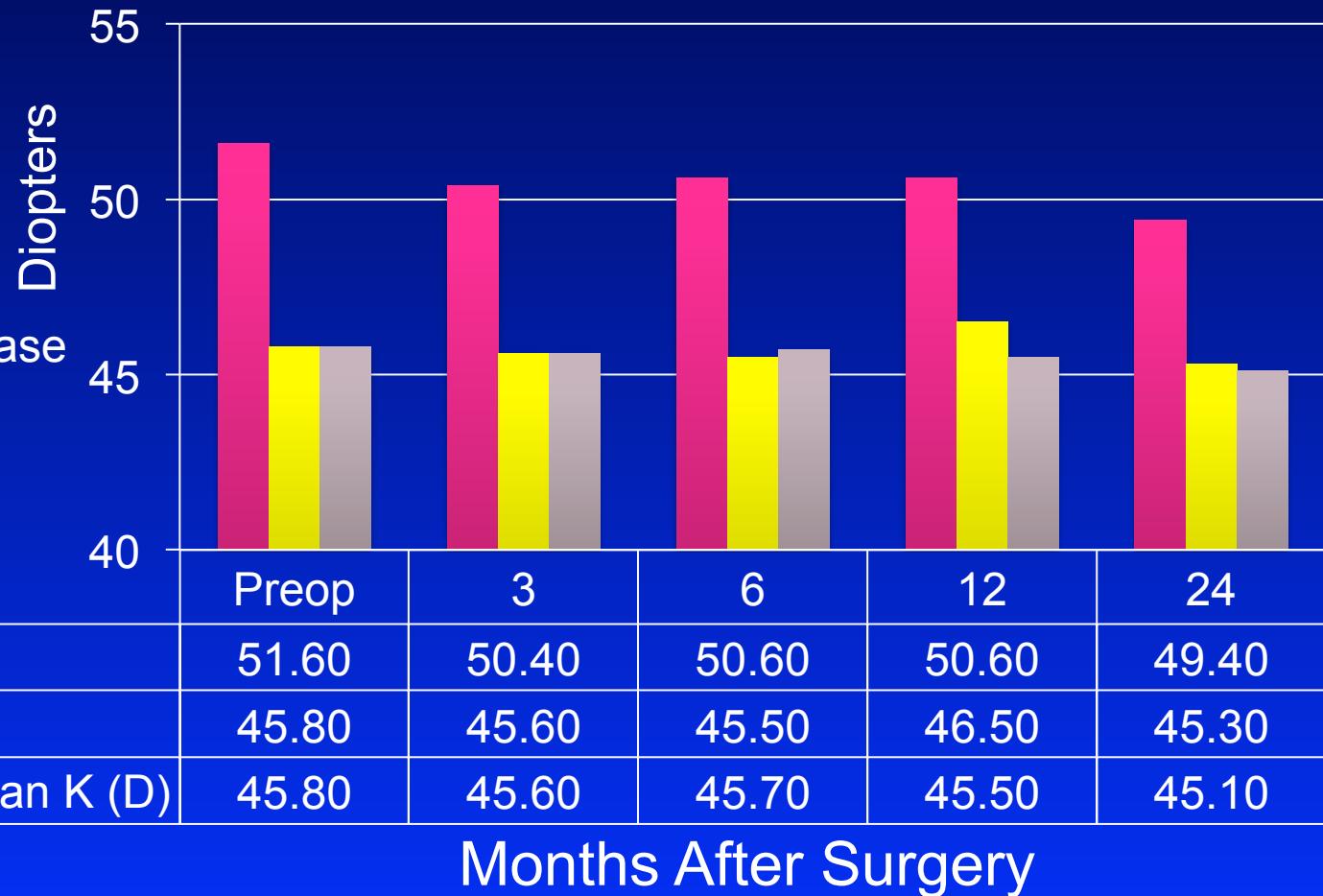


Subject ATL-003 OD

14 yof with Keratoconus

Kmax ↓ 2.2 D

Continued decrease
from 1-2 years



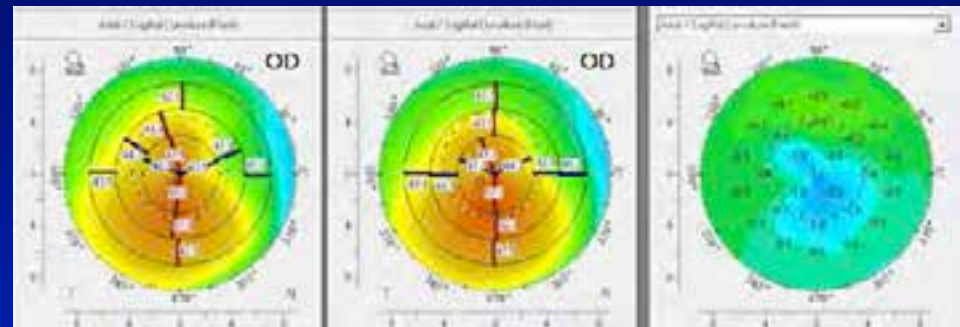
Case Reports

Subject ATL-124

10 yo hispanic female with KC

Right Eye

Visit Type	UCVA	BCVA
Pre-Op	20/200	20/40
3 Months	20/40	20/40
6 Months	20/25	20/25
12 Months	20/25	20/25



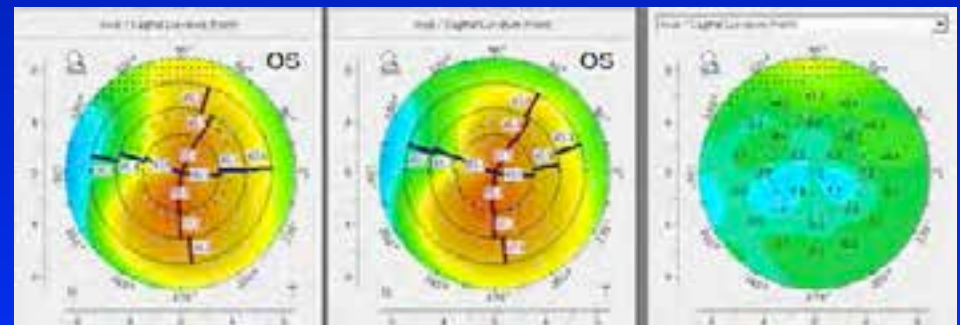
12 months

preop

difference

Left Eye

Visit Type	UCVA	BCVA
Pre-Op	20/80	20/30
3 Months	20/60	20/50
6 Months	20/40	20/25
12 Months	20/30	20/25



Subject ATL-078

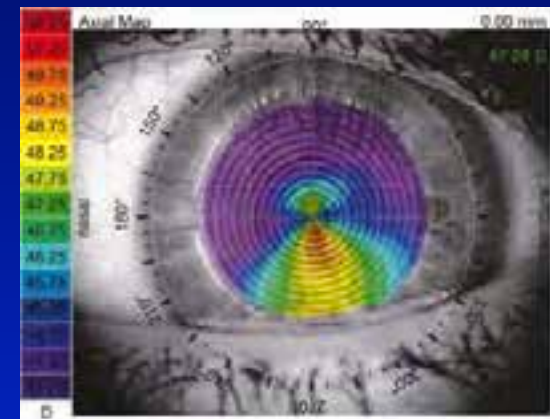
OD Not treated



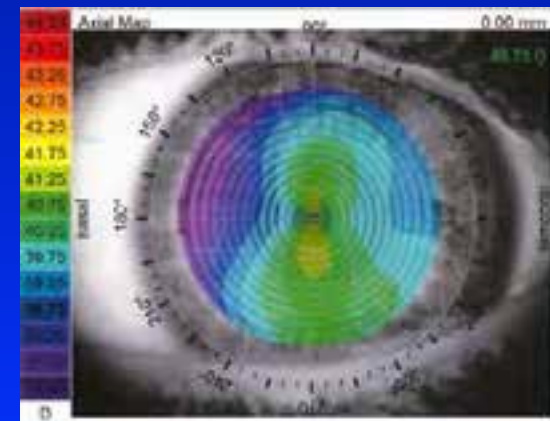
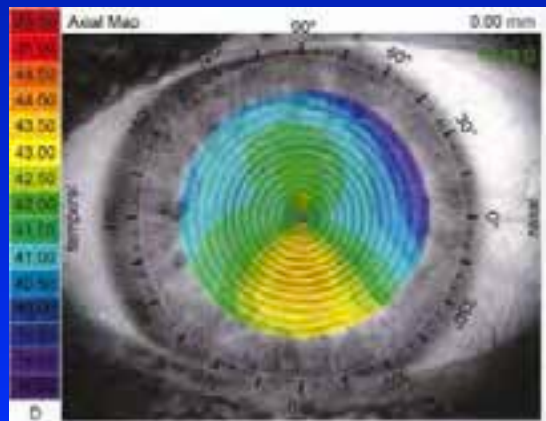
4/15/14
20/20 BSCVA 20/40 BSCVA

2 ½ years

OS CXL 5/8/14



11/3/16
20/20 BSCVA 20/20 BSCVA



Re-Treatments

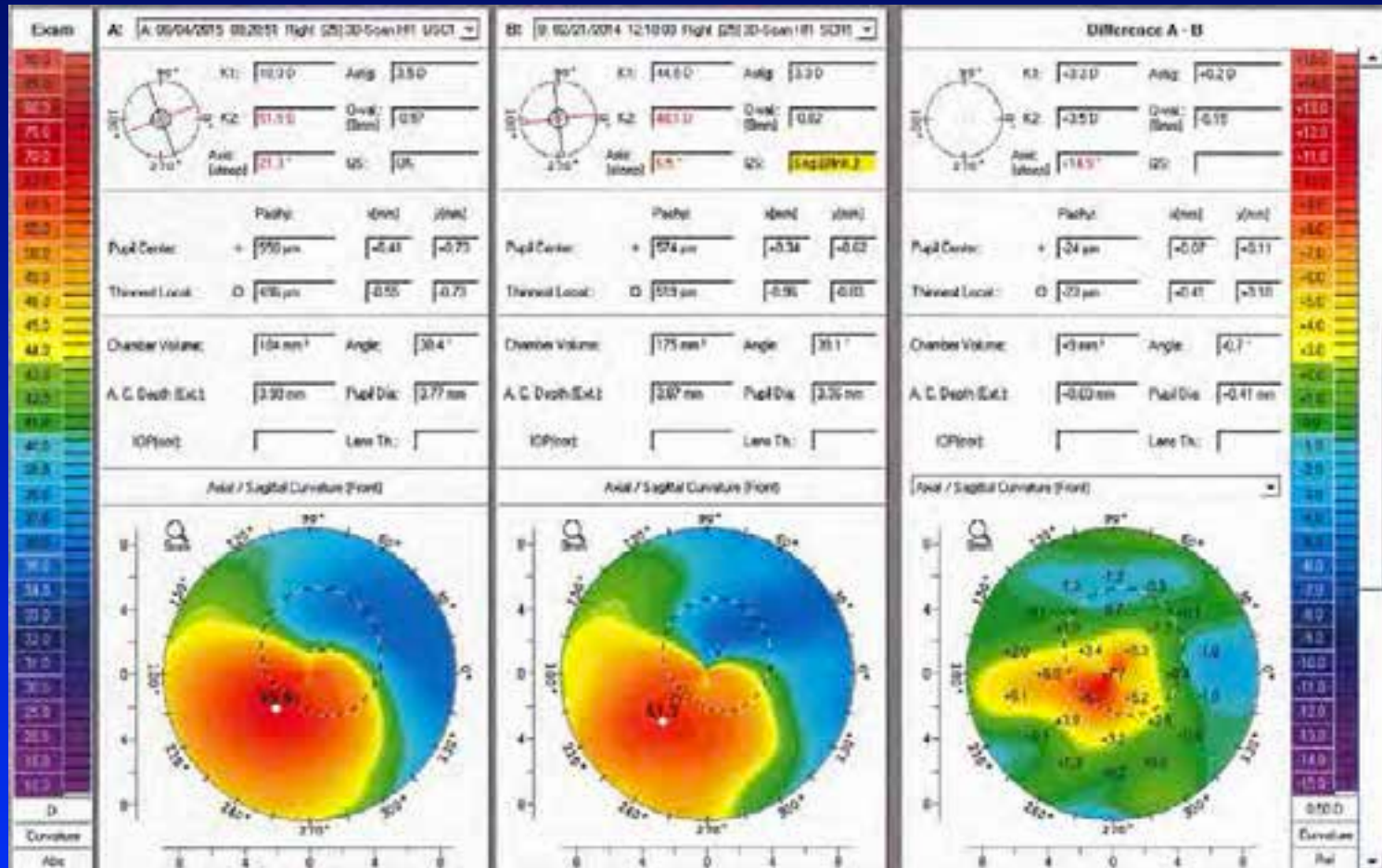
1 eye during study

1 eye after study

Subject ATL-054 OD

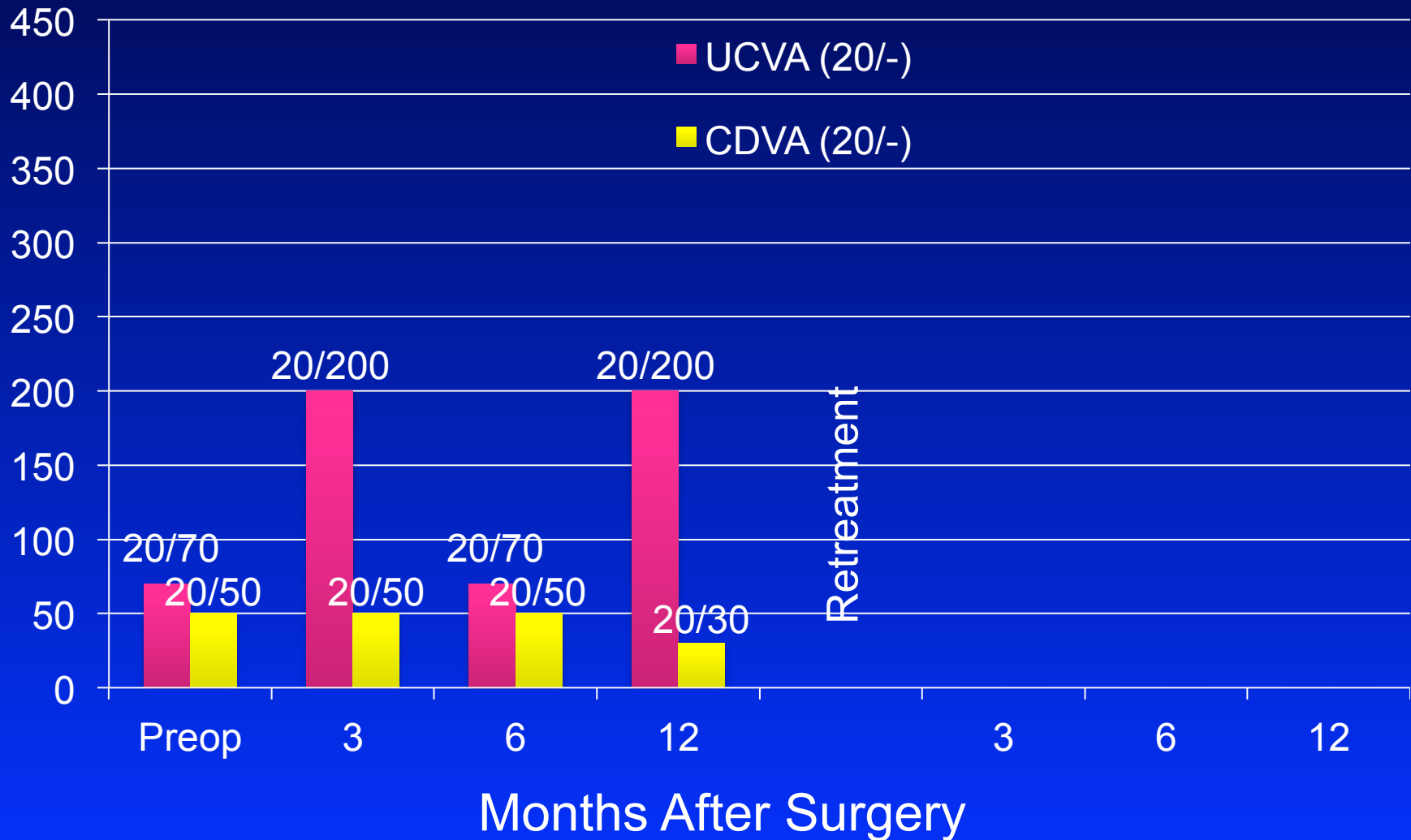
16 yom with Keratoconus

12 months



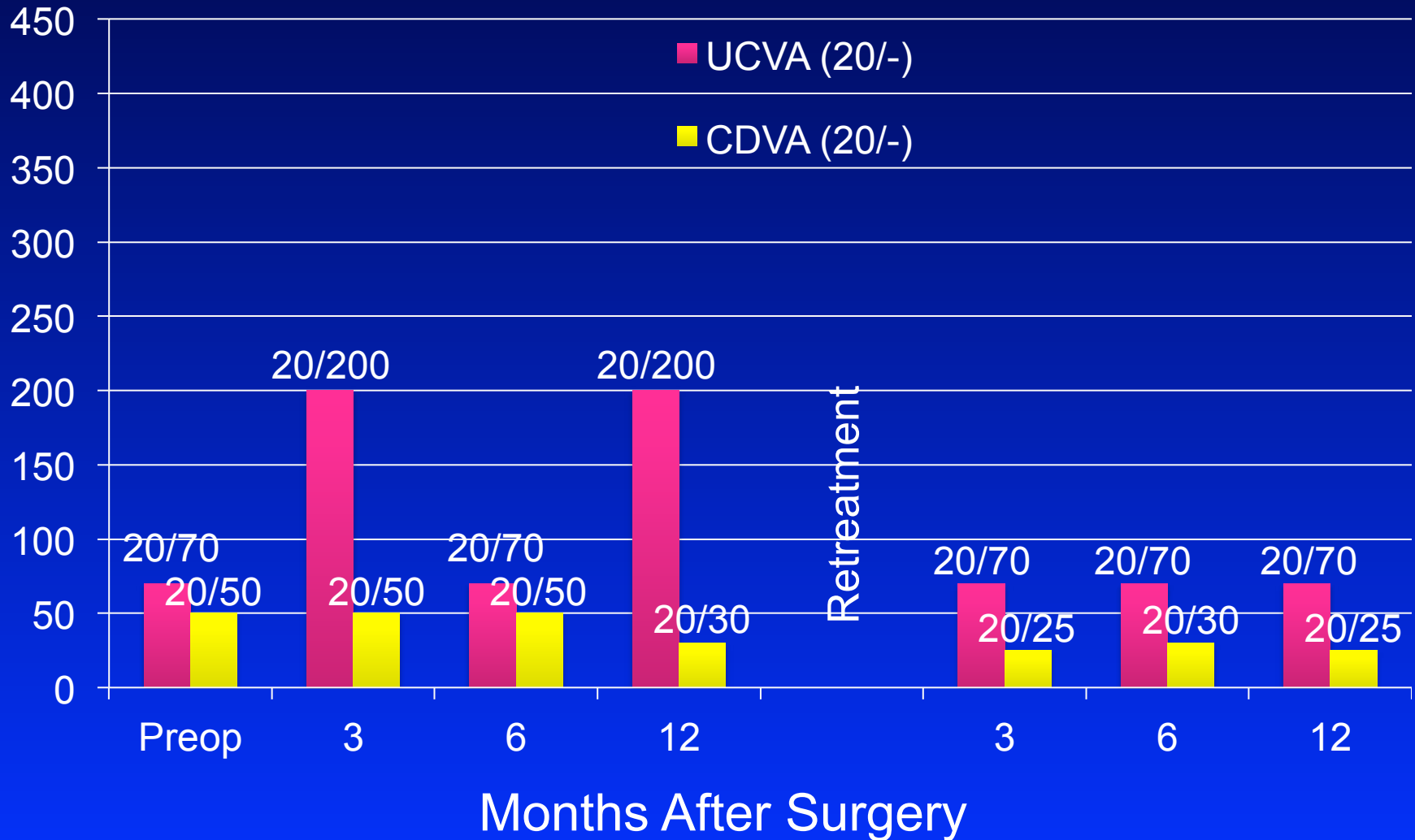
Subject ATL-054 OD

16 yom with Keratoconus



Subject ATL-054 OD

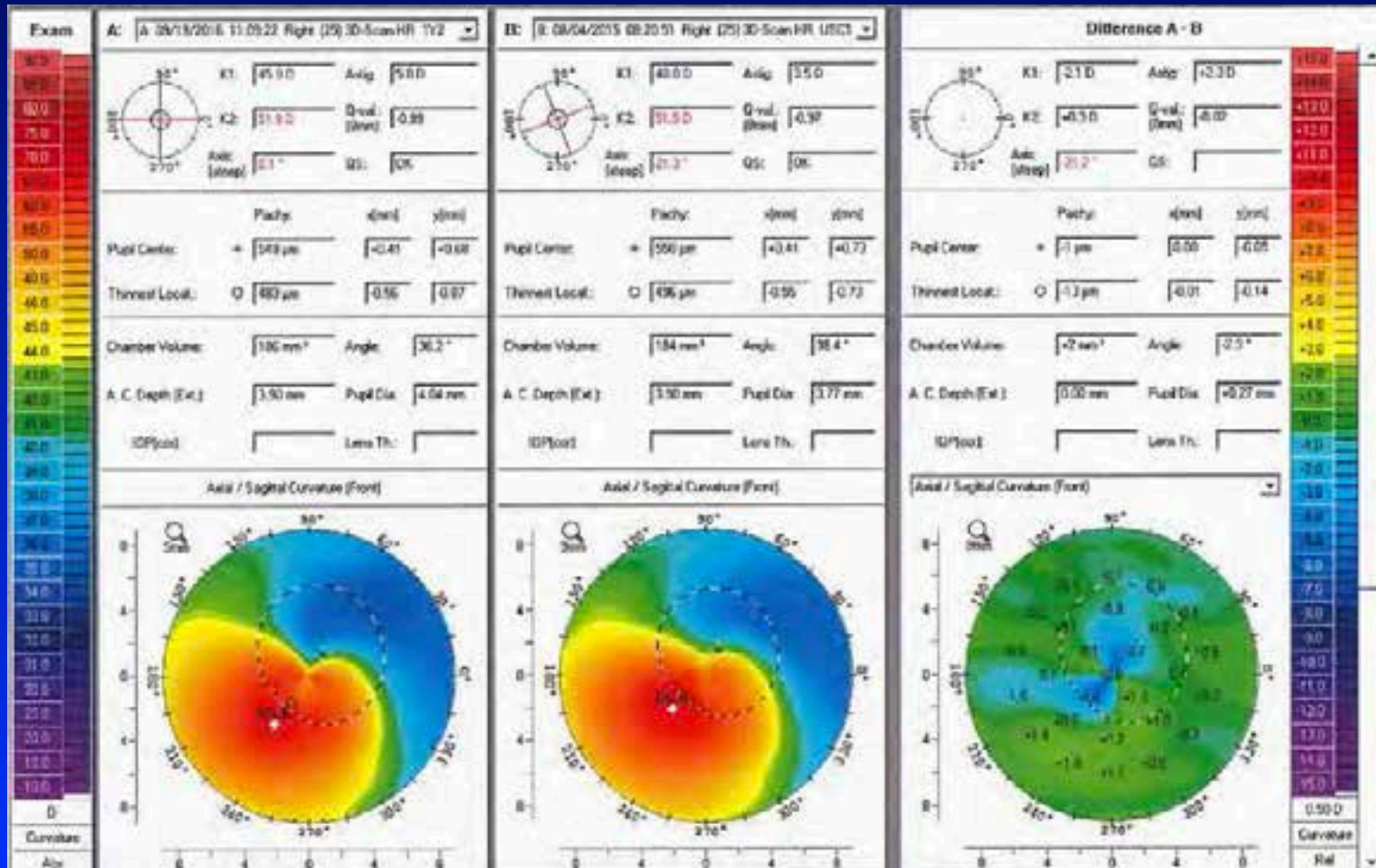
16 yom with Keratoconus



Subject ATL-054 OD

16 yom with Keratoconus

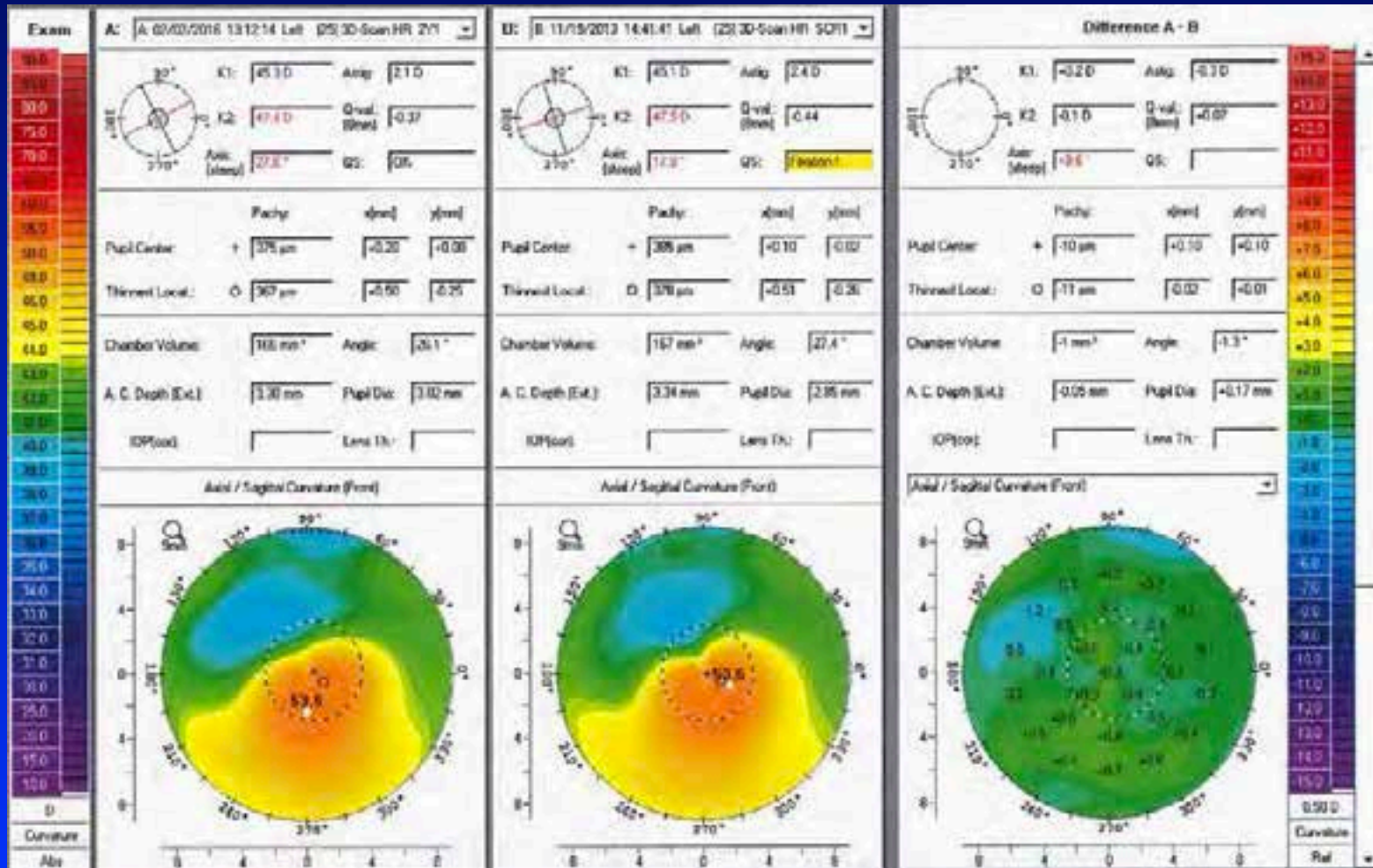
12 months after re-treatment



Subject ATL-028 OS

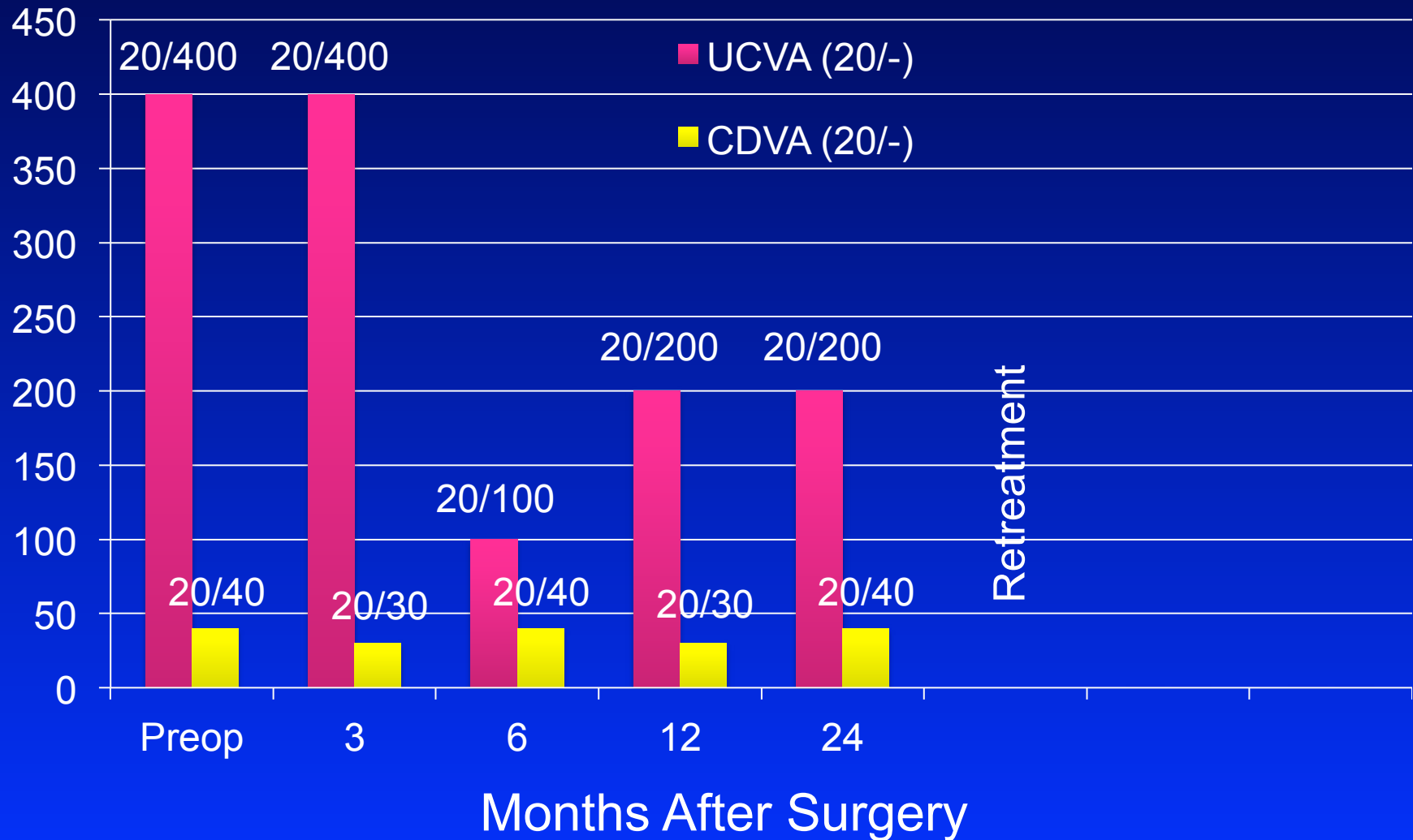
58 yof with Ectasia

24 months



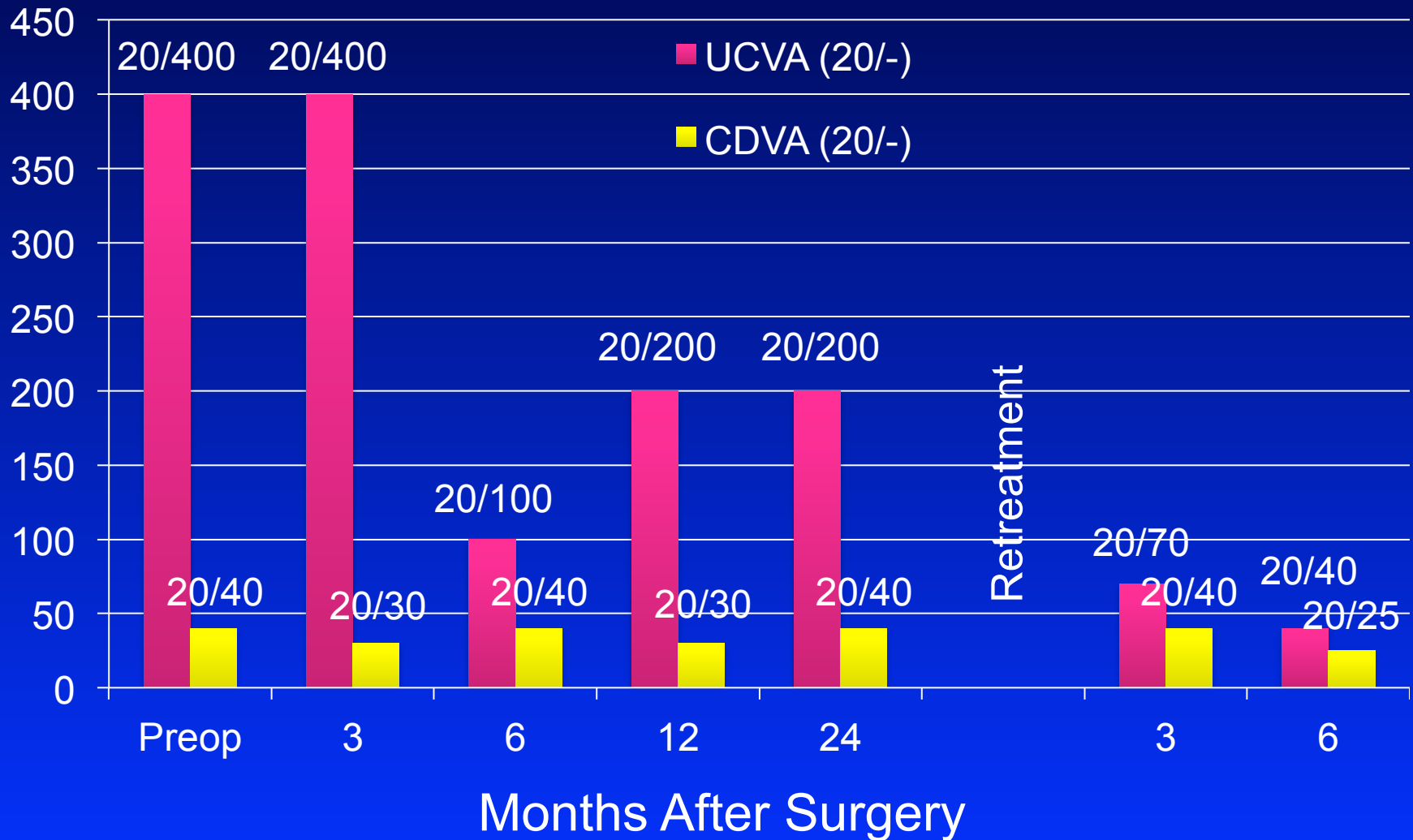
Subject ATL-028 OS

58 yof with Ectasia



Subject ATL-028 OS

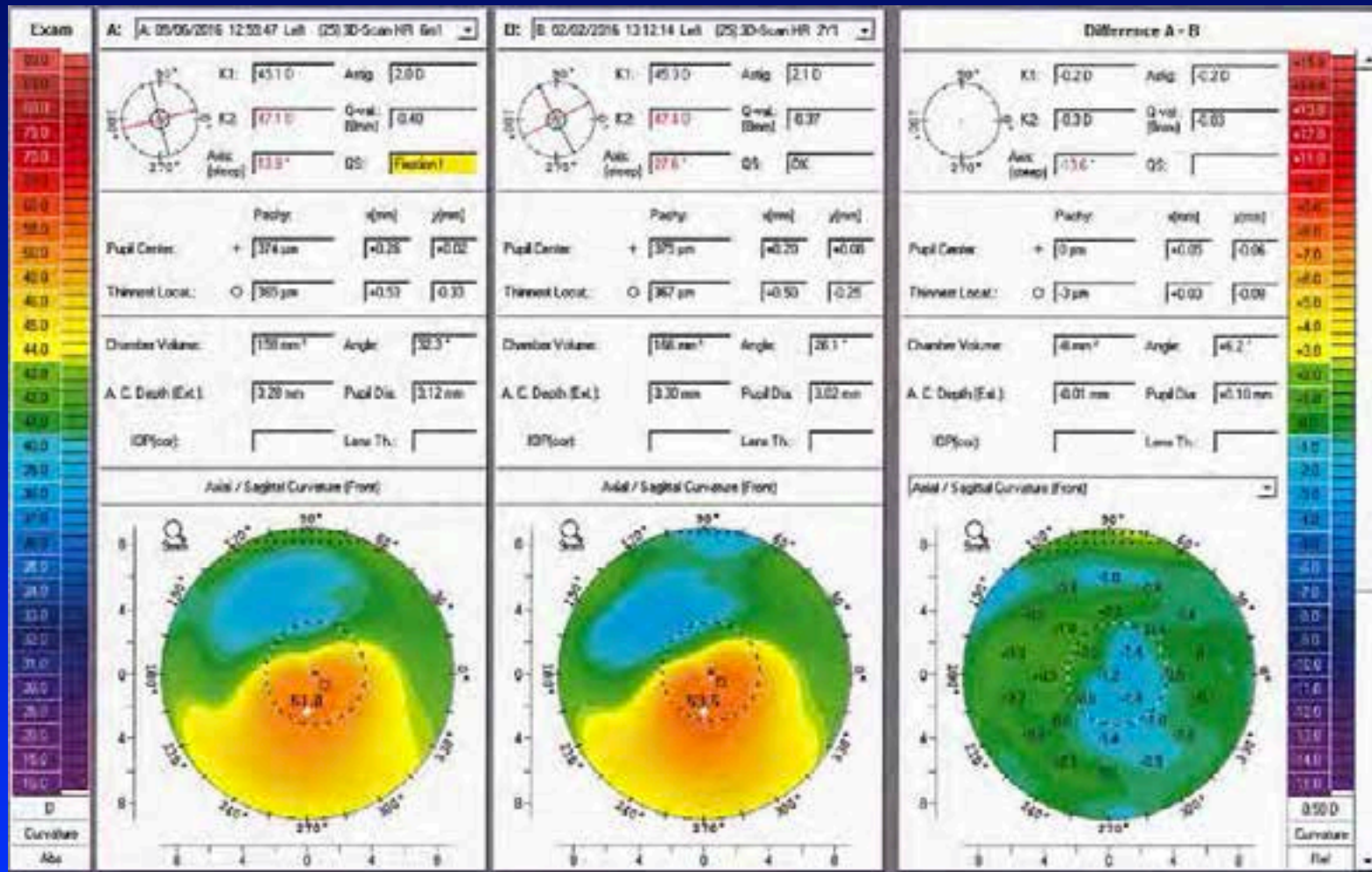
58 yof with Ectasia



Subject ATL-028 OS

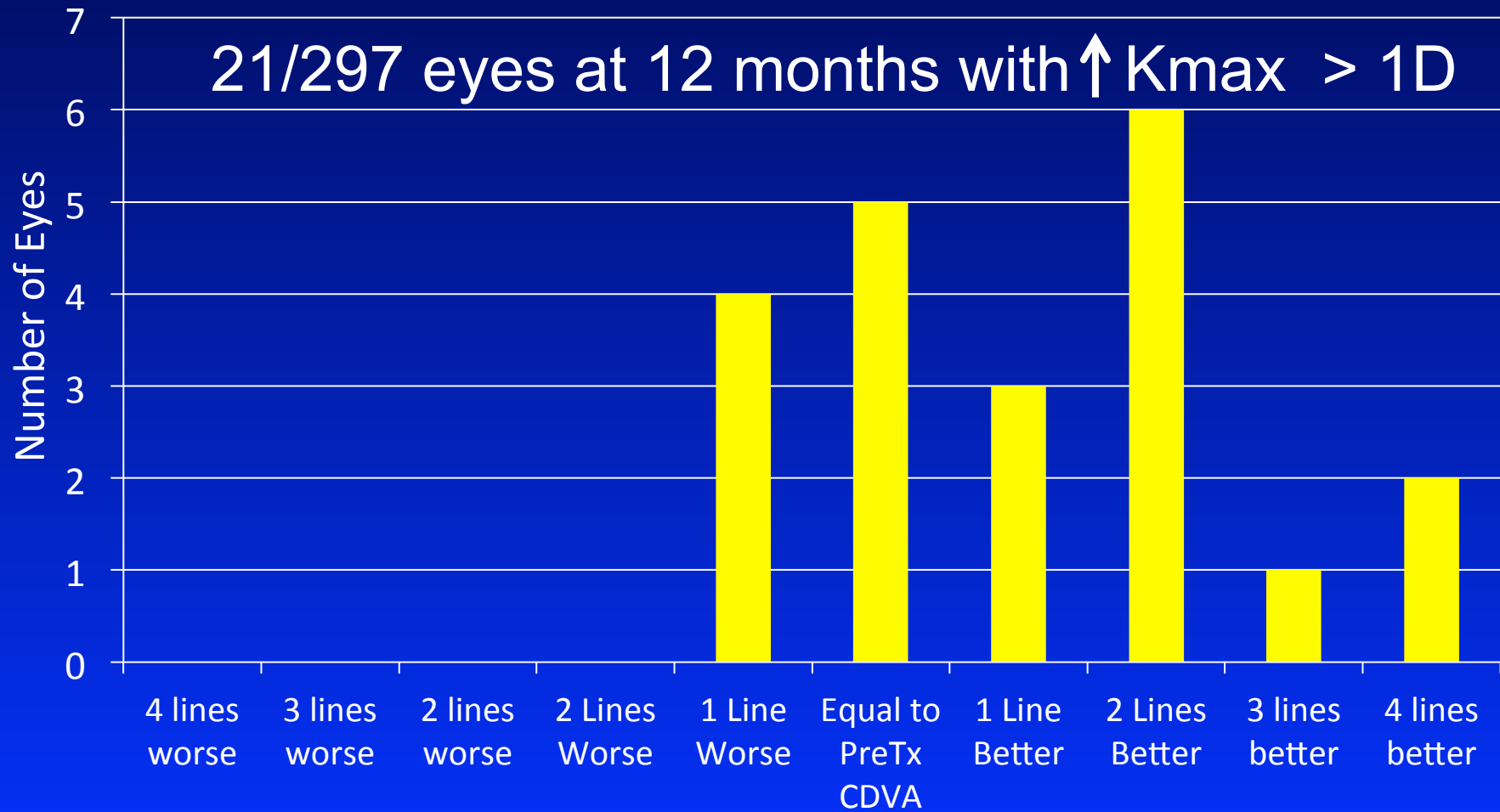
58 yof with Ectasia

6 months after re-treatment

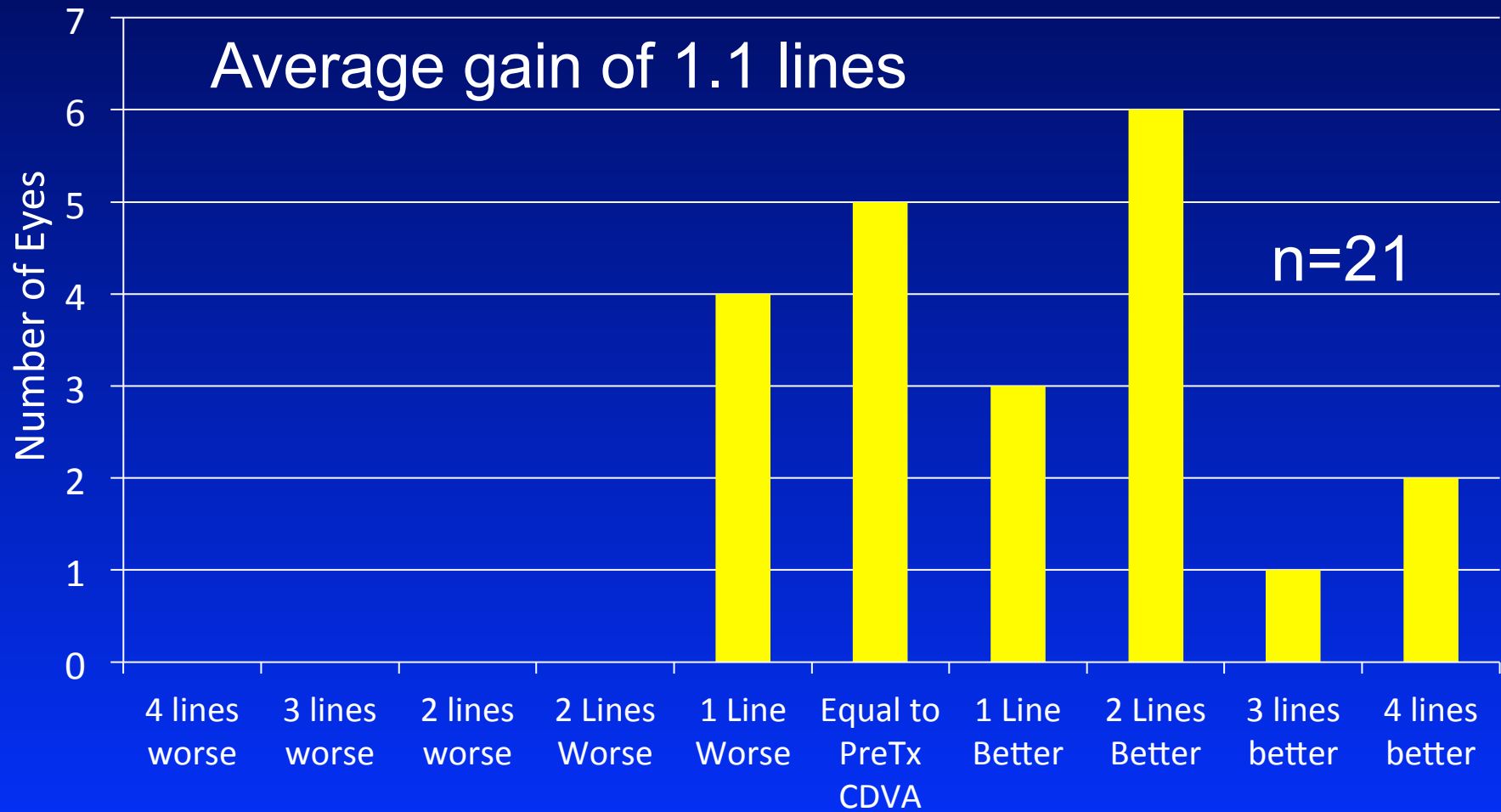


What About Eyes With An
Increase In K_{max} ?

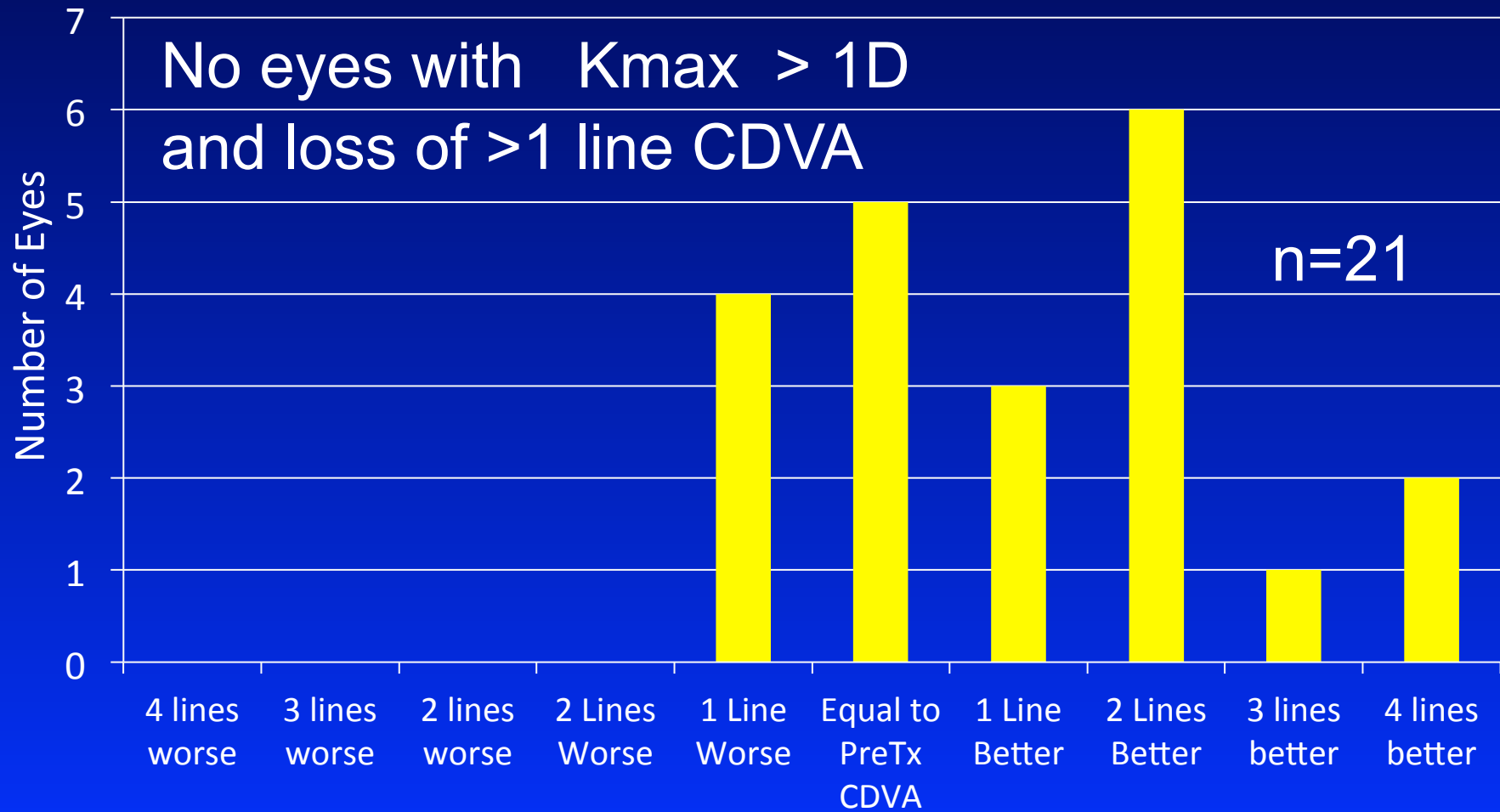
CDVA When $\uparrow K_{max} > 1D$ at 12 mos



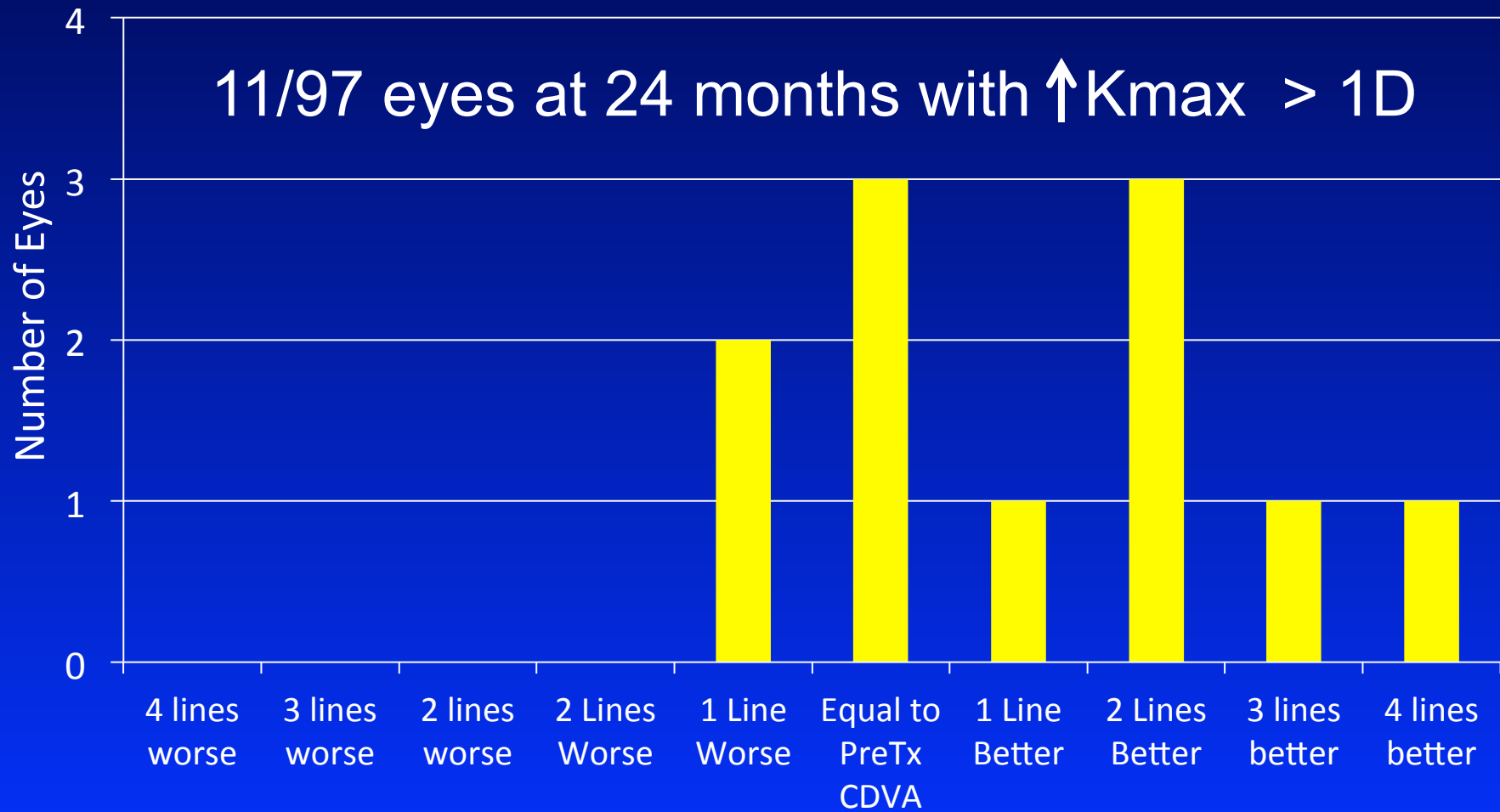
CDVA When $\uparrow K_{max} > 1D$ at 12 mos



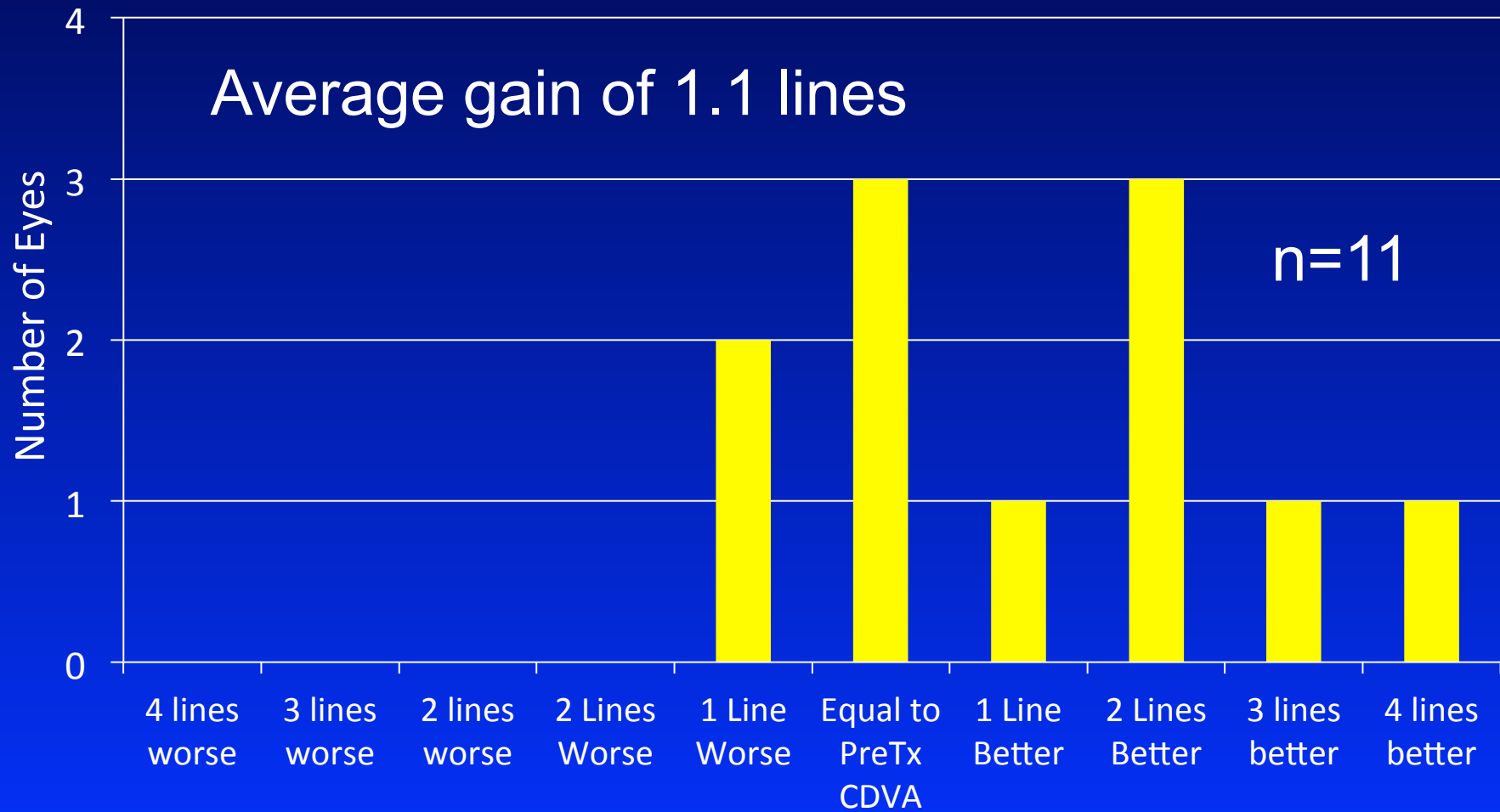
CDVA When $\uparrow K_{max} > 1D$ at 12 mos



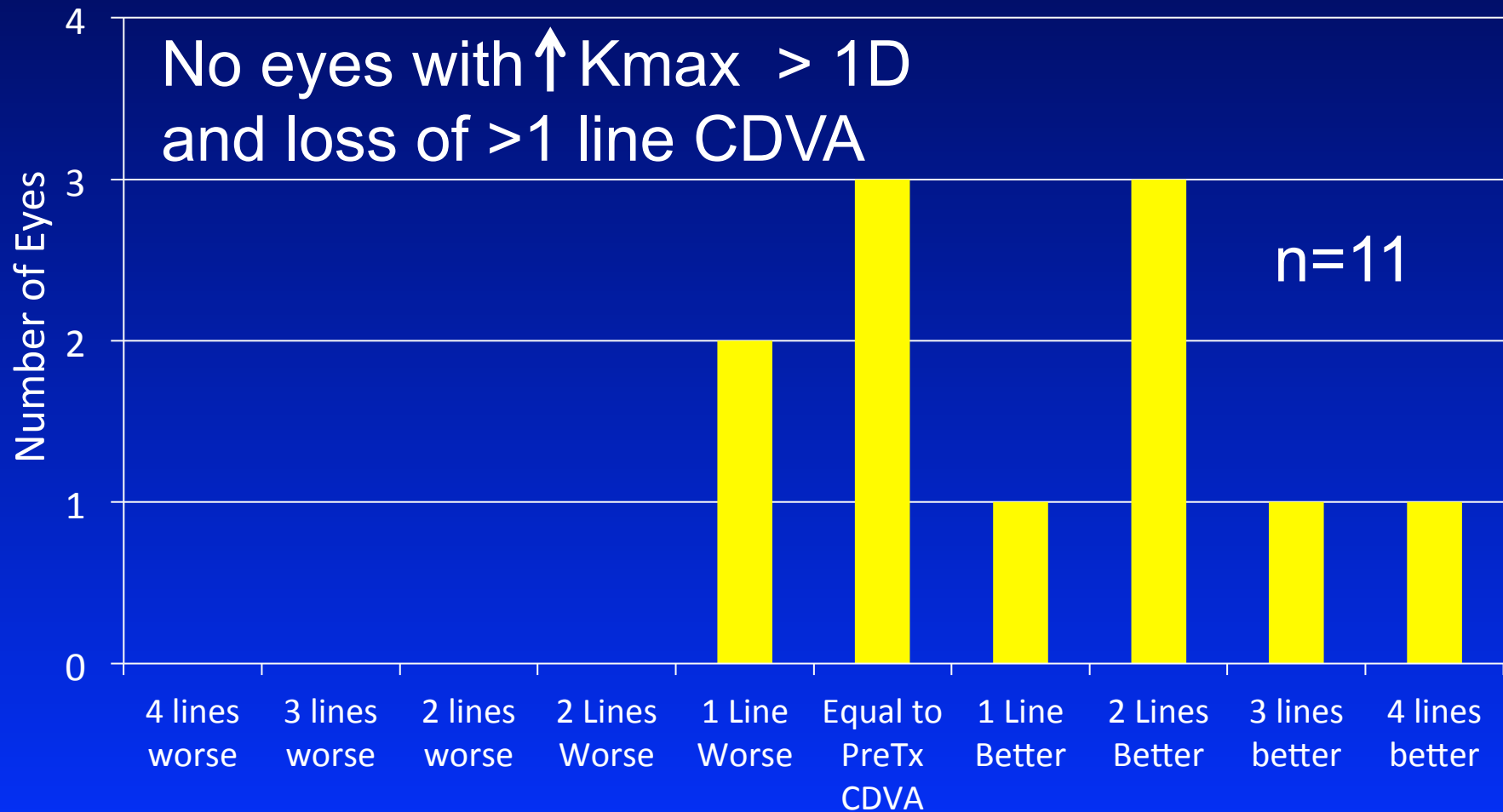
CDVA When $\uparrow K_{max} > 1D$ at 24 mos



CDVA When $\uparrow K_{max} > 1D$ at 24 mos



CDVA When $\uparrow K_{max} > 1D$ at 24 mos



Adverse Events

Adverse Events

ATL-051 OD

- Hydrops
 - » 1 eye with ectasia at 23 months
 - » Underwent PK

	UCVA	CDVA	Kmax ¹
Preop	20/400	20/400	72.0
24 months	20/400	20/200	79.4

¹Data gaps on all Pentacam exams

Adverse Events

ATL-185 OS

- Scleritis
 - » 1 eye with KC at 3 weeks
 - » Responded to oral steroids

	UCVA	CDVA	Kmax
Preop	20/50	20/25	58.5
24 months	20/30	20/20	59.1

Adverse Events

ATL-037 OD

- Disciform edema
 - » 1 eye with KC at 15 mos
 - » On Valtrex 500 mg qd for oral HSV
 - » Responded to Valtrex 1 gm BID and topical steroids

	UCVA	CDVA	Kmax
Preop	20/400	20/30	58.2
24 months	20/400	20/20	56.7

Conclusions

- Epi-on CXL using CXLO technologies halts progression of ectatic corneal disease without loss of effect between 1 and 2 years
- Improvement in CDVA is similar to that with epi-off CXL
- No complications of epithelial removal
- No eyes with $> 1D$ increase in K_{max} and loss of > 1 line CDVA
- No AE's resulting in visual loss
- K_{max} may not be best metric for evaluating CXL

Thank You



Differences In Technique

- BAC or Tris + EDTA
- No physician assessment of saturation
- Riboflavin during UVA exposure
- 9 mm diameter light
- Continuous UVA
- 3 mW/cm²
- Novel riboflavin formulation¹
- Physician SL verification and saturation as needed
- No riboflavin during UVA exposure
- 12 mm diameter light
- Pulsed UVA
- 4 mW/cm²

¹Patented riboflavin with optimized osmolarity, pH, concentration, non-toxic additive and delivery system developed by CXL Ophthalmics

Demarcation Lines

CXLUSA

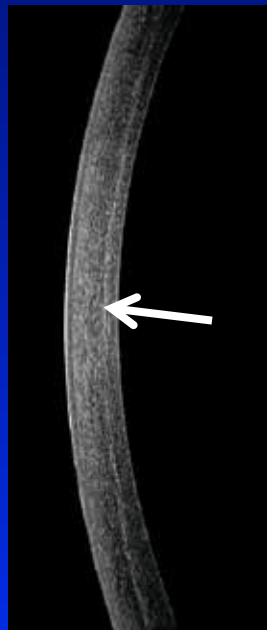
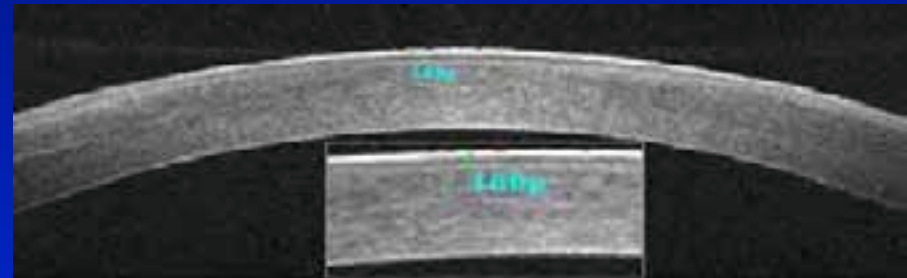


Photo Courtesy of Dan
Goodman, MD

0.1% Riboflavin + THAM + EDTA



Filipello, JCRS 2012;38:238

Slit Lamp Grading System

Grade 0/V



Grade I/V



Slit Lamp Grading System

Grade II/V



Grade III/V

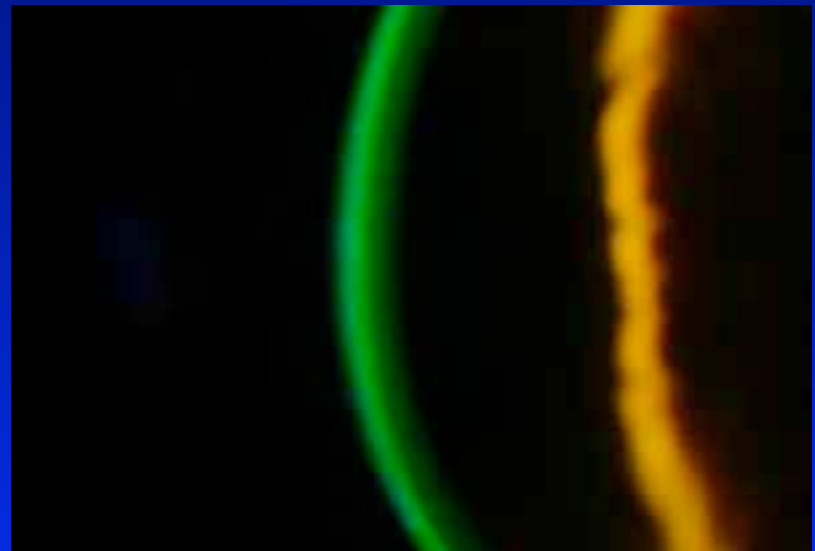


Slit Lamp Grading System

Grade IV/V

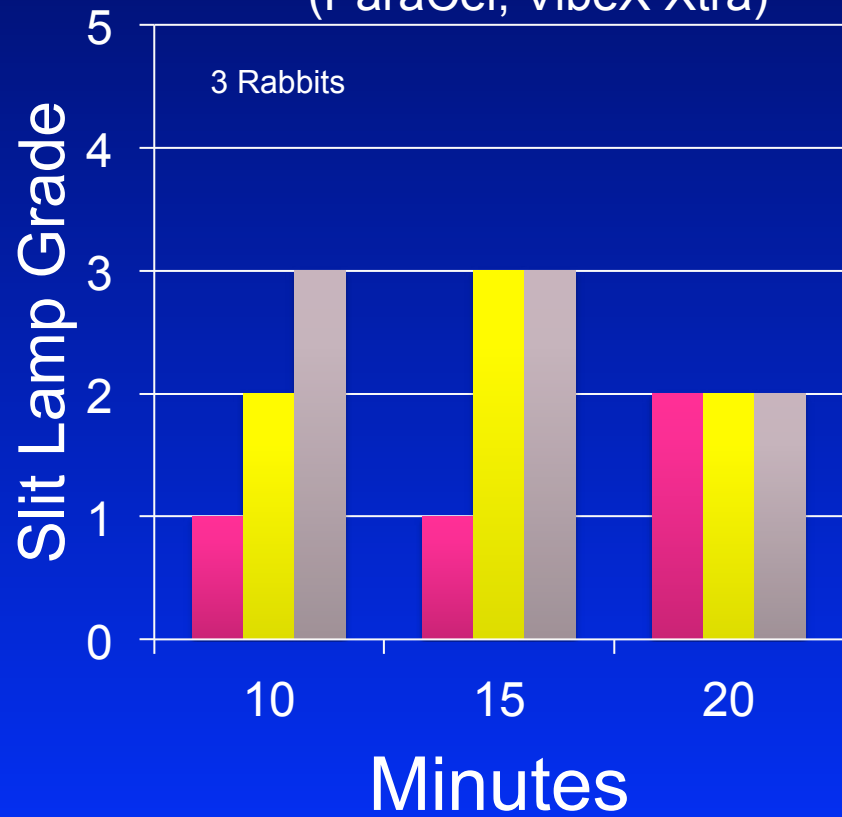


Grade V/V

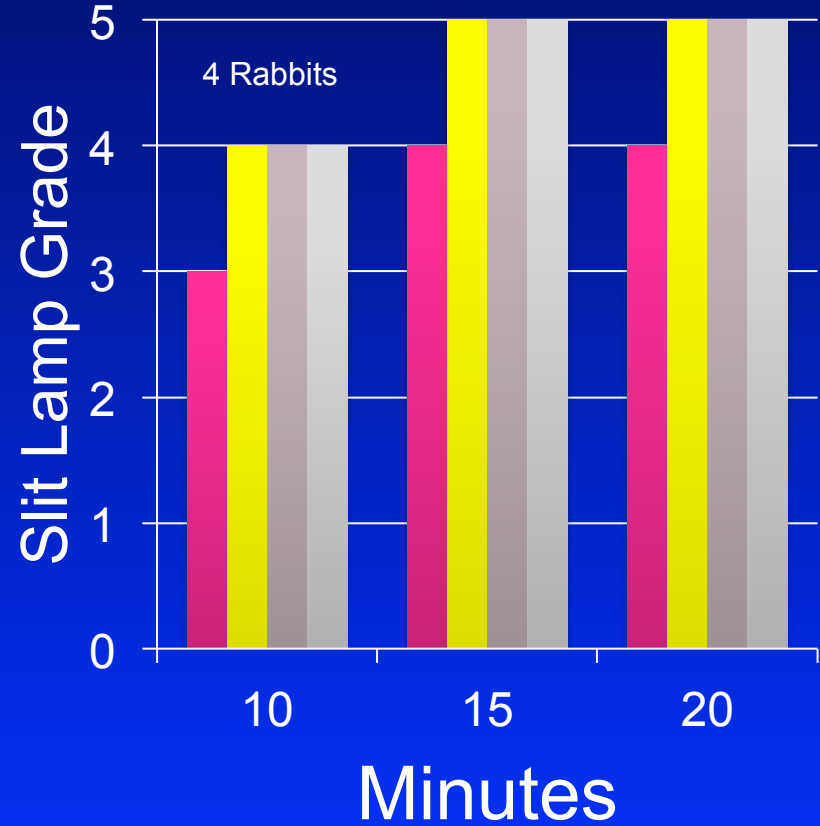


Slit Lamp Grade

Commercially Available Formulation
(ParaCel, VibeX Xtra)



CXLUSA Formulation



SLE vs Riboflavin Concentration

